

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Daniel E. Afar et al. Examiner: G. Nickol  
Serial No.: Group Art Unit: 1642  
Filed: June 21, 2001 Docket: G&C 129.18-US-D1  
Title: BPC-1: A SECRETED BRAIN-SPECIFIC PROTEIN EXPRESSED AND  
SECRETED BY PROSTATE AND BLADDER CANCER CELLS

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By:

Name: Isabell Ogata

PRELIMINARY AMENDMENT

Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

Prior to a first Office Action, please amend the above-identified application as follows. Please note that the amended paragraphs of the specification are presented in clean form with marked-up versions provided in the Appendix.

IN THE SPECIFICATION

At page 1, line 3, please insert the following paragraph:

This application is a divisional of United States patent application number 09/374,135, filed August 10, 1999, which application claims the benefit of United States provisional application number 60/095,982, filed August 10, 1998, now abandoned.

Please replace the paragraph at page 5, lines 14-16, with the following paragraph:

FIG. 1(A-C). Molecular structure of human BPC-1: Nucleotide and deduced amino acid sequences of BPC-1 clone 6 cDNA (SEQ ID NOS: 1 and 2, respectively). The signal sequence is indicated in boldface, the CUB domain in underlined boldface, and the SSH-derived nucleic acid sequence in boldface.

Please replace the paragraph at page 5, lines 23-27, with the following paragraph:

FIG. 3. Molecular structure of human BPC-1: Amino acid sequence alignment of the BPC-1 CUB domain with CUB domains from various known proteins. (A) Alignment of BPC-1 with C. elegans CUB domain protein (SEQ ID NO: 3; Wilson et al., 1994, Nature 368:32-38), and (B) alignments with the CUB domains of murine BMP-1 (SEQ ID NOS: 4-8; Fukagawa et al. 1994, Dev. Biol 163: 175-183). Percent sequence identities are indicated on the figure.

Please replace the paragraph at page 5, lines 32-33, with the following paragraph:

FIG. 5. Semi-quantitative RT-PCR expression analysis showing human BPC-1 expression in prostate cancer xenografts (lanes 3-5 of panel A) and a limited number of normal human tissues (lanes 1-2 of panel A; lanes 1-8 of panels B and C).

Please replace the paragraph at page 7, lines 6-11, with the following paragraph:

FIG. 15. BPC-1-AP binds to a 45 kDa protein using a far-western analysis. Lysates from brain, testis, prostate, the xenografts LAPC4AD and LAPC9AD, and the cell lines 3T3, LAPC4, LNCaP, and PC-3 were used to make the western blots. The blots were incubated with conditioned media from a 293T cell line producing only secreted alkaline phosphatase (B) and with media containing BPC-1-AP (A). The alkaline phosphatase signals were detected using a chemiluminescent AP detection system.

Please replace the paragraphs at page 35, lines 20-36, with the following paragraphs:

DPNCDN (cDNA synthesis primer) (SEQ ID NO: 9):

5'TTTTGATCAAGCTT<sub>30</sub>3'

Adaptor 1 (SEQ ID NO: 10):

5'CTAATACGACTCACTATAGGGCTCGAGCGGCCGCCCCGGGCAG3'  
3'GGCCCGTCCTAG5'

Adaptor 2 (SEQ ID NO: 11):

5'GTAATACGACTCACTATAGGGCAGCGTGGTCGCGGCCGAG3'  
3'CGGCTCCTAG5'

PCR primer 1 (SEQ ID NO: 12):

5'CTAATACGACTCACTATAGGGC3'

Nested primer (NP)1 (SEQ ID NO: 13):

5'TCGAGCGGCCGCCCCGGGCAGGA3'

Nested primer (NP)2 (SEQ ID NO: 14):

5'AGCGTGGTCGCGGCCGAGGA3'

Please replace the paragraphs at page 38, lines 11-20, with the following paragraphs:

5'- TGC CGT ATG TCA CTG TCT CTA GGT -3' (SEQ ID NO: 15)  
5'- GAA ATC ATG GGT ATT TCA TGT GCT -3' (SEQ ID NO: 16)

These primers were designed from the sequence of the SSH fragment of the initially isolated 19P1E8 gene. Use of the following primer pair, based on sequences within the open reading frame of the 19P1E8 gene, produced the same expression pattern.

5'- CTC CCA ACT ATC CCA GCA AGT ATC-3' (SEQ ID NO: 17)  
5'- AAA TCC CAT AGA TTC CAG CTC TCC -3' (SEQ ID NO: 18)

Please replace the paragraphs at page 48, lines 5-9, with the following paragraphs:

GTGTAAGCTTCCACCAAGAAAGGAACAGAA (SEQ ID NO: 19)

BPC1.BAMHI PRIMER:

CACAGGATCCCTTACCAGGTGTGAAATTG (SEQ ID NO: 20)

#### IN THE CLAIMS

Please cancel claims 6-15.

## REMARKS

Prior to a first Office Action in this application, Applicants request that original claims 6-15 be canceled and that the specification be amended as indicated above. In addition, Applicants request that the application be amended to include the paper copy of the Sequence Listing submitted herewith, which Sequence Listing is identical to that which was submitted on February 3, 2000, in the parent application, number 09/374,135, filed August 10, 1999. In accordance with 37 CFR 1.821(e), please use the (only) computer readable form of the Sequence Listing filed in application number 09/374,135 as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make the necessary change in application number and filing date for the instant application.

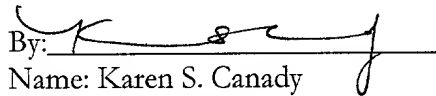
These amendments, including the Sequence Listing, do not involve new matter or objectionable changes.

It is submitted that this application is now in good order for allowance and such allowance is respectfully solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

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By:   
Name: Karen S. Canady  
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KSC/io  
G&C 129.18-US-D1

APPENDIX : AMENDED SPECIFICATION IN MARKED-UP FORM

At page 1, line 3, please insert the following paragraph:

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